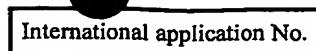
PATENT COOPERATION TREATY



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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Anslation inter	PATENT COOPERATE PCT	•	ATY PCT/EP2003
TSIA.			
INTE	RNATIONAL PRELIMINARY	EXAMIN.	ATION REPORT
	(PCT Article 36 and	d Rule 70)	· · · · · · · · · · · · · · · · · · ·
Applicant's or agent's file reference A2002/00656	FOR FURTHER ACTION	See Notifi Preliminary	cation of Transmittal of Internati Examination Report (Form PCT/IPEA/4
International application No.	International filing date (day)	•	Priority date (day/month/year)
PCT/EP2003/003973	16 April 2003 (16.0	4.2003)	29 April 2002 (29.04.2002)
A61K 9/127, 9/16, 31/3	(IPC) or national classification and IPC 55, 31/015		
Applicant	BIOTESYS GM	вн	
amended and are the 70.16 and Section (accompanied by ANNEXES, i.e., sheets ne basis for this report and/or sheets cont 607 of the Administrative Instructions unsist of a total of 4 sheets.	aining rectification ander the PCT).	ion, claims and/or drawings which have ations made before this Authority (see
3. This report contains indicate	ations relating to the following items:		
I Basis of the	he report		
II Priority	•		
III Non-estat	olishment of opinion with regard to nove	lty, inventive	step and industrial applicability
	nity of invention		
v Reasoned citations	l statement under Article 35(2) with rega and explanations supporting such statem	rd to novelty, ent	inventive step or industrial applicability;
VI Certain d	ocuments cited		
VII Certain d	efects in the international application		
VIII Certain o	bservations on the international applicat	ion	
Date of submission of the deman	d Date	e of completion	n of this report
	003 (13.11.2003)	24	September 2004 (24.09.04)
Name and mailing address of the	IPEA/EP Aut	horized officer	
Facsimile No.	Tele	phone No.	·
T. GPOHITH C 140.			المساور والمراوي والم



PCT/EP2003/003973

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

I.	Basis (of the re	port	
1.	With	regard to	the elements of the international application:*	
		the inte	rnational application as originally filed	·
	冈	the des	cription:	
	<u>~</u>	pages	1-16	, as originally filed
		pages		, filed with the demand
		pages	, filed with the letter of	
	∇	the clai		
			itis.	, as originally filed
		pages	as amended (together v	vith any statement under Article 19
		pages pages	, (((((((, filed with the demand
		pages	1-23 , filed with the letter of	13 May 2004 (13.05.04)
		_	, III de William de la companya de l	
	\boxtimes	the dra		on onicinally filed
		pages	1/2-2/2	, as originally filed , filed with the demand
		pages		, filed with the demand
		pages	, filed with the letter of	
	t t	he seque	nce listing part of the description:	
-		pages		, as originally filed
		pages		, filed with the demand
		pages	, filed with the letter of	
	the in These	the land the land or 55.3 regard minary e	to any nucleotide and/or amino acid sequence disclosed in the internation was carried out on the basis of the sequence listing:	which is: e 23.1(b)). examination (under Rule 55.2 and/
	Θ		ned in the international application in written form. See ther with the international application in computer readable form.	
			ed subsequently to this Authority in written form.	
			ed subsequently to this Authority in computer readable form.	
		The s	atement that the subsequently furnished written sequence listing does not	go beyond the disclosure in the
		The st	tional application as filed has been furnished. atement that the information recorded in computer readable form is identical turnished.	to the written sequence listing has
4.		The ar	nendments have resulted in the cancellation of:	
ı			the description, pages	•*
			the claims, Nos.	
		П	the drawings, sheets/fig	
5.	\boxtimes	This rebeyond	port has been established as if (some of) the amendments had not been made, single the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**	ce they have been considered to go
*	in th	acement is repor 10.17).	sheets which have been furnished to the receiving Office in response to an invitati t as "originally filed" and are not annexed to this report since they do not	ion under Article 14 are referred to contain amendments (Rule 70.16
**			ent sheet containing such amendments must be referred to under item 1 and annex	ed to this report.



International application No.

PCT/EP2003/003973

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

		stablishment of opinion with regard to novelty, inventive step and industrial applicability
1.	The quindustri	lestions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be ially applicable have not been examined in respect of:
		the entire international application.
	\boxtimes	claims Nos
	because	e:
		the said international application, or the said claims Nos relate to the following subject matter which does not require an international preliminary examination (specify):
ı		
	\boxtimes	the description, claims or drawings (indicate particular elements below) or said claims Nos3 are so unclear that no meaningful opinion could be formed (specify):
•		
		the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed.
		no international search report has been established for said claims Nos.
	2. A me	eaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid ence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
		the written form has not been furnished or does not comply with the standard.
		the computer readable form has not been furnished or does not comply with the standard.
1		

International application No.

PCT/EP 03/03973

I. Basis of the report

1. This report has been drawn on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

5.

The new set of claims submitted with the fax of 13 May 2004 fails to meet the requirements of PCT Article 19(2) because the content of claim 1 goes beyond the disclosure in the international application as filed. The term "substance" is broader than the original term "active substance". Furthermore, a basis for the use of the term "liposome" could not be found.

For these reasons, this report has been established without taking the submitted amendments into account.

International application No.
PCT/EP 03/03973

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1

The phrase "chemically inert substance such as, for example, nanoparticles such as carbon nanotubes, nanothreads, colloids, etc." used in claim 3 is unclear and leaves the reader uncertain as to the meaning of the technical features involved. Consequently, the definition of the subject matter of this claim is not clear (PCT Article 6).

Furthermore, is not clear whether conjunction between "amino acids" and "chemically inert substance" should be "and" or "or".

International application No.

PCT/EP 03/03973

v.	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
	citations and explanations supporting such statement

Statement			
Novelty (N)	Claims	9, 11, 14-19, 22	YES
	Claims	1-2, 4-8, 10, 12-13, 20-21, 23-24	NO
Inventive step (IS)	Claims	11	YES
•	Claims	9, 14-19, 22	NO
Industrial applicability (IA)	Claims	1-2, 4-24	YES
	Claims		NO

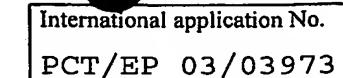
2. Citations and explanations

The prior art documents are numbered according to their order in the research report.

1) Novelty

The content of claims 1, 2, 4-8, 10, 12-13, 20-21 and 23-24 is not novel within the meaning of PCT Article 33(2). D1 describes a selective transport system consisting of liposomes, peptides being coupled to the phospholipid layer of said liposomes via a polyethylene oxide spacer (see abstract, figure 2 and page 242, column 1, second paragraph). The modified liposomes are used for the selective transport of an active substance to particular cells of the organism (see page 245, column 1, second and third paragraphs). The docking of the liposome modified with a linear RGD peptide to integrin GPIIb-IIIa is selected as a model example of selective transport (see abstract). The RGD peptide with the sequence GSSSGRGDSPA comprises sequence ID NO: 1 specified in claim 8, the sequence section Arg-Gly-Asp (= RGD) being responsible for the bond to the integrin (see page 240, column 1, third paragraph).

D2 describes active substance-containing phospholipid liposomes whose surfaces are occupied by ligands that bind



to specific cells (see claims 23-43). Sterile barriers are used as spacers between the liposome and ligand (see claims 42-43). Liposomes modified in this manner are suitable as transport systems for active substances such as anti-tumor agents, anesthetics, beta-blockers, antibiotics, antidepressants, vitamins, enzymes or immunostimulating agents (see page 30, line 20 to page 31, line 32). These liposomes can generally be loaded with any product (see page 32, line 20-23).

The content of claims 1-2, 4-8, 10, 12-13, 20-21 and 23-24

2) Inventive step

is therefore not novel.

The content of claims 9, 14-19 and 22 does not involve an inventive step within the meaning of PCT Article 33(3). The problem addressed by the present application is that of providing a better system for the target-oriented biological transport of active substances. The solution is a liposome with attached oligopeptides whose sequences are binding sites for proteins. Since in D1, peptides with the RGD sequence have already been used successfully with liposomes for specifically binding to integrin GPIIb-IIIa, and thus for the targeted use of anticoagulants, a person skilled in the art can directly and clearly deduce that liposomes that are derived with specific peptide sequences for binding to retinal cells can be used for the target-controlled transport of active substances to the retina. The sequences 9 to 15 disclosed in the present application are subsequences of R-cadherin (see D4), which is a protein for cell-to-cell adhesion for the retina. It is therefore obvious for a person skilled in the art to couple this peptide to the liposome for targeted administration to the retina.

International application No.

PCT/EP 03/03973

Since D1 clearly states that any active substance can be administered via modified liposomes, the administration of micronutrients such as vitamins or trace elements via modified liposomes does not involve an inventive step because a surprising and unexpected effect is not discernible.

The content of claims 9, 14-19 and 22 is therefore not inventive.

3) Industrial applicability

The content of claims 1-2 and 4-24 is industrially applicable within the meaning of PCT Article 33(4).